Resistance Exercise Impacts Lean Muscle Mass in Women with Polycystic Ovary Syndrome

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ABSTRACT

KOGURE, G. S., C. L. MIRANDA-FURTADO, R. C. SILVA, A. S. MELO, R. A. FERRIANI, M. F. S. DE SÁ, and R. M. DOS REIS. Resistance Exercise Impacts Lean Muscle Mass in Women with Polycystic Ovary Syndrome. Med. Sci. Sports Exerc., Vol. 48, No. 4, pp. 589–598, 2016. Purpose: This study investigated the effects of progressive resistance training (PRT) on lean muscle mass (LMM) in women with or without polycystic ovary syndrome (PCOS) and its effects on metabolic factors and concentrations of related steroid hormones. Design: This was a nonrandomized, therapeutic, open, single-arm study. Participants: All in all, 45 sedentary women with PCOS and 52 without (non-PCOS), 18–37 yr of age, with body mass indexes (BMI) of 18–39.9 kg m⁻² of all races and social status, performed PRT three times a week for 4 months. Before and after PRT, the concentrations of hormones and metabolic factors and waist circumference were measured. LMM and total body fat percentage were determined using dual-energy x-ray absorptiometry. Clinical characteristics, LMM, and fasting glucose were adjusted for confounding covariables and compared using general linear mixed models. Each patient’s menstrual history was taken before study enrollment and after PRT. Results: PRT resulted in reduced plasma testosterone and fasting glucose levels. After PRT, the androstenedione concentration increased and the sex hormone-binding globulin concentration decreased in women with PCOS. The waist circumference was reduced (P < 0.01) and the muscle mass index, lean mass (LM)/height², increased in women with PCOS (P = 0.04). Women with PCOS showed increased muscle mass indexes of appendicular LM/height² (P = 0.03) and LM/height² (P < 0.01) compared with the baseline. Total LM and trunk LM were elevated in women with PCOS (P = 0.01) at the baseline and after PRT. Conclusion: To our knowledge, this is the first report to show that resistance exercise alone can improve hyperandrogenism, reproductive function, and body composition by decreasing visceral fat and increasing LMM, but it has no metabolic impact on women with PCOS. Key Words: PROGRESSIVE RESISTANCE TRAINING, FASTING GLUCOSE, REPRODUCTIVE FUNCTION, STRENGTH TRAINING

Polycystic ovary syndrome (PCOS) is a heterogeneous clinical condition characterized by hirsutism, irregular menstruation, chronic anovulation, and endocrine disorders such as hyperandrogenism that affects 7%–14% of women of reproductive age (28). PCOS is associated with metabolic syndrome, obesity, type 2 diabetes (T2D), and cardiovascular disease risk factors (33). Both lean and obese women with PCOS have a general tendency toward android fat distribution patterns (26). This excess central fat is associated with increased low-grade chronic inflammation and insulin resistance (IR) (6); in this same context, IR is exacerbated by an increased BMI (39).

The literature to date has primarily highlighted the role of excessive adipose tissue as a cause of IR (6), whereas lean muscle mass (LMM) contributes to metabolism and is a primary target of insulin and androgens (12). Muscle mass is believed to promote insulin sensitivity because it is responsible for up to 80% of the insulin-dependent glucose uptake (14). LMM may be an important body composition parameter for the assessment of PCOS. This trend may be increased in women with PCOS, in whom factors such as obesity, IR, and excessive androgens are frequently present and may play a role in increased LMM (7).

Physical inactivity, weight gain, and genetic predisposition play an important role in the clinical expression of PCOS (41). In 2011, the PCOS Australian Alliance published the first evidence-based guidelines for its assessment and management, recommending moderate- to high-intensity aerobic activities to improve clinical results (42), prevent metabolic complications, reestablish ovulation, and increase the likelihood of pregnancy (47).

Interventions such as strength training or progressive resistance training (PRT) have been recommended by the
American College of Sports Medicine and American Diabetes Association as an integral component of a daily exercise routine for healthy adults for the prevention and treatment of chronic noncommunicable diseases (10). PRT can improve strength and muscle mass and reduce the risks of sarcopenia, IR, and bone mineral density loss (13). PRT is increasingly recognized as an important component in the treatment of T2D (40) because of its effects on metabolic dysfunction in skeletal muscle (48). Androgens are important muscle mass regulators and are considered anabolic hormones, which induce muscle mass increases by stimulating and/or inhibiting protein synthesis (3). Adaptations to strength training are influenced by changes in hormone concentrations due to various types of stimuli applied in weight training, including volume, intensity, resting intervals, and muscle groups used (38). Increased metabolic hormone secretions may contribute to the chronic adaptations (muscle hypertrophy) caused by this type of training.

A recent review article presented evidence that PRT may be beneficial to women with PCOS (9); however, no reports to date have demonstrated the efficacy of this training type in women with PCOS. Therefore, we evaluated the efficacy of PRT for increasing LMM in women with PCOS versus those without PCOS and improving metabolic factors and concentrations of related steroid hormones in women with PCOS.

METHODS

Ethics statement. This nonrandomized, therapeutic, open, single-arm study was approved by the Institutional Review Board of the University Hospital (UH) of the Ribeirão Preto Medical School, University of São Paulo (process number 13475/2009). All participants provided written informed consent. In addition, all trials ongoing and related to this intervention were registered in the Brazilian Clinical Trials Registry under RBR-7p23c3.

Recruitment and eligibility. Participants were consecutively recruited between February 2010 and December 2013. Women with PCOS were selected from the outpatient clinics of the Human Reproduction sector of the Department of Gynecology and Obstetrics at the UH of Ribeirão Preto Medical School, University of São Paulo, and from basic health clinics throughout the city. Healthy controls (non-PCOS) were recruited from among women seen for routine gynecological examinations at the UH and basic health clinics and through public advertisements in the local newspaper and on regional television. The inclusion criteria were as follows: female sex, 18–37 yr of age, any race, any social status, sedentary or did not engage in regular supervised physical activity, and BMI indicating a normal weight status (18–25 kg/m²) or an overweight status (25–29.0 kg/m²) or first-degree obesity (>30 kg/m²) according to the World Health Organization criteria. The exclusion criteria included the presence of systemic diseases, hormonal contraceptive use, smoking, and pregnancy. Participants who did not complete the study were excluded from the analysis.

After recruitment, participants completed the physical activity readiness questionnaire (44) before any inferences, or quantitative assessments were performed to determine whether a medical evaluation was required. Participants underwent transvaginal pelvic ultrasonography examinations with a Voluson 730 Expert machine (GE Medical Systems, Zipf, Austria) to evaluate the presence of polycystic ovaries. For the diagnosis of PCOS, peripheral blood samples were collected, and concentrations of thyroid-stimulating hormone (TSH), 17-hydroxyprogesterone (17-OHP), prolactin, and testosterone were measured. Based on these results, the participants were assigned to the PCOS or non-PCOS groups.

The diagnosis of PCOS involves a variety of biochemical and clinical phenotypes. The PCOS group (n = 45) was classified using the Rotterdam consensus (43), which defines four distinct phenotypes that may differ in the metabolic risk profile: 1) anovulation + hyperandrogenism; 2) anovulation + polycystic ovaries; 3) hyperandrogenism + polycystic ovaries; and 4) anovulation + hyperandrogenism + polycystic ovaries (16). The non-PCOS group (n = 52) consisted of healthy women with regular menstrual cycles of 24–32 d and flow duration of 3–7 d.

Anthropometric measurements and evaluations of LMM and total body fat percentage. Body weight and height were measured to the nearest 0.1 kg and 0.5 cm, respectively, using standardized equipment and procedures (Filizola, São Paulo, Brazil). Each patient’s BMI was calculated as their weight in kilograms divided by the square of the height in meters. Each patient’s waist circumference (WC) was measured at the midpoint between the lateral iliac crest and the lowest rib margin at the end of normal expiration. LMM and body fat percentage (%BF) were determined using total body dual-energy x-ray absorptiometry (QDR Discovery® Series; Hologic Devices, Bedford, MA). The LMM measures used in this analysis included the following: total lean mass (LM) (g), trunk LM (g), muscle mass index (LM/height²), and appendicular LM (appLM/height²), which is calculated as the sum of the muscle mass of the right and left arms and legs. The latter are indexes based on the total LM and not on the body weight and are normalized in relation to height that can be calculated with the 5 Discovery Wi model (S/N 84826) software version 13.0 provided by the manufacturer.

Biochemical measurements. The concentrations of FSH (sensitivity [S], 0.1 mU/mL⁻¹; intra- and interassay coefficients of variation [CV], 2.9%–4.1%), luteinizing hormone (LH) (S, 0.05 mU/mL⁻¹; intra- and interassay CV, 3.6%–6.7%), prolactin (S, 0.5 ng/mL⁻¹; intra- and interassay CV, 3.3%–4.8%), estradiol (S, 15 pg/mL⁻¹; intra- and interassay CV, 9.9%–16%), sex hormone-binding globulin (SHBG) (S, 0.02 nmol/L⁻¹; intra- and interassay CV, 2.7%–5.2%), TSH (S, 0.004 mIU/mL⁻¹; CV, 3.9%–4.8%), and fasting insulin (S, 2 μIU/mL⁻¹; CV, 5.5%–7.3%) were assessed using chemiluminescence (Immulite®2000 Immunoassay System; Siemens®, Santa Ana, CA). Testosterone
(S, 0.1 ng·mL\(^{-1}\); intra- and interassay CV, 3.1%–11.2%), androstenedione (S, 0.3 ng·dL\(^{-1}\); intra- and interassay CV, 6.3%–7.0%), and 17-OHP (S, 0.07 ng·mL\(^{-1}\); intra- and interassay CV, 7.1%–7.3%) concentrations were measured using a radioimmunoassay (Immulite® 1000 Immunoassay System; Siemens®). The plasma glucose level was determined with the glucose oxidase method. The free androgen index (FAI) was determined using total testosterone (nmol·L\(^{-1}\)/SHBG (nmol·L\(^{-1}\)) × 100 (8), and IR was quantified using the homeostatic model assessment of IR (HOMA-IR) ([fasting glycemia level (mg·dL\(^{-1}\)) × 0.05551 × [fasting insulin level (µIU·mL\(^{-1}\)])/22.5] (31). Baseline TSH and 17-OHP levels were assessed, and all other characteristics were measured before and after PRT. Venous blood samples were drawn after a 10-h overnight fast and at least 48 h after the training sessions.

**PRT.** PRT was performed at the Centre of Physical Education, Recreation, and Sports at the University of São Paulo. The volunteers received training for familiarization with the exercises and underwent an adaptation period of 2 wk or six adaptation sets; the initial load intensity of all exercises after the adaptation period was based on dynamic maximum muscle strength based on the one-repetition maximum test (32) (see document, Supplemental Digital Content 1, progressive resistance training, http://links.lww.com/MSS/A603).

Volunteers performed PRT for strength and hypertrophy according to recommendations for adult beginners of the American College of Sports Medicine (1). Physical education professionals supervised each exercise, and a linear periodization of training was prepared that followed a trend of decreasing volume and increasing intensity throughout the training period. In this training protocol, the exercise intensity was increased in each microcycle, whereas the number of repetitions was decreased (maintaining a minimum of eight repetitions) because of increased overload. The exercises included bench presses, leg extensions, front lat pull-downs, leg curls, lateral raises, leg presses (45°), triceps pulleys, calf leg presses, arm curls, and abdominal exercises executed in alternating segments. The training duration program for each participant was approximately 1 h·d\(^{-1}\) three times a week for 4 months.

During this training period, the observed results for all measured outcomes were presented to each participant. We provided a Centre of Physical Education, Recreation, and Sports membership, light meal after each PRT session, and a pair of running shoes to increase participant compliance and adherence. The outcome measurements described below were obtained before and after completion of the PRT program. Exercise adherence was monitored through direct supervision, and data were recorded by physical education professionals. The criterion of nonaccession was failure to attend at least 20% or eight training sessions of the programmed training sessions. The subjects were instructed not to undertake any regular or supervised exercise during the PRT duration.

**Menstrual history.** Menstrual history was recorded before study enrollment and after PRT. The history included questions relating to menstruation regularity such as the number of days from the beginning of one menstrual period to the beginning of the next menstrual period as well as and the number of days of the menses (4).

**Statistical analysis.** The optimal sample size was calculated based on previously published data on muscular strength in young women using bench presses (29.54 ± 5.37 kg), leg extensions (41.09 ± 18.78 kg), and arm curls (16.00 ± 3.13 kg) (34); we calculated that a minimum of 120 participants (60 per group) were needed to observe a 10% mean difference between groups, have 80% statistical power, and a significance level of 0.05. A total of 170 volunteers were recruited to prevent a negative impact of potential losses.

Student’s t-test was used to independently compare the mean variables between groups. Clinical characteristics, % BF, LMM, and LM index were compared using general linear mixed models (random and fixed effects), where random effects control the correlations between repeated measures (i.e., more than one measurement for the same participant). The data were logarithmically transformed for cases in which the residues were not normally distributed. Planned orthogonal contrasts were used for posttest comparisons. Age, BMI, and HOMA-IR scores were used as covariates for all analyses; training time (before and after training) and study groups (non-PCOS and PCOS) were independent variables. The correlations between LM and HOMA-IR in the LM variable that differed between periods (the delta was the post-minus preintervention results) were examined using bivariate (Pearson) correlation. All statistical analyses were performed using SAS® 9.0 (SAS Institute Inc., University of North Carolina, Cary, NC), and values of \( P < 0.05 \) were considered statistically significant. The data are presented as mean (SD) and 95% confidence interval (CI) where appropriate.

**RESULTS**

The study’s chronogram and flow chart are shown in Figures 1 and 2, respectively. The age distribution between groups was homogeneous (PCOS 28.1 ± 5.4 yr vs non-PCOS 29.6 ± 5.2 yr, \( P = 0.22 \)). Concentrations of prolactin (PCOS 13.8 ± 9.7 ng·mL\(^{-1}\) vs non-PCOS 14.8 ± 10.4 ng·mL\(^{-1}\), \( P = 0.15 \)), 17-OHP (PCOS 117.6 ± 78.1 ng·dL\(^{-1}\) vs non-PCOS 111.5 ± 71.6 ng·dL\(^{-1}\), \( P = 0.62 \)), and TSH (PCOS 2.35 ± 1.4 µIU·mL\(^{-1}\) vs non-PCOS 2.04 ± 1.1 µIU·mL\(^{-1}\), \( P = 0.88 \)) did not differ significantly between groups. There were 15 and 27 participants with normal BMI in the PCOS and non-PCOS groups, respectively, whereas 15 and 11 were overweight and 15 and 14 participants were obese, respectively. According to the four PCOS phenotypes defined by the Rotterdam criteria, phenotype 1 was present in four women, phenotype 2 in six women, phenotype 3 in 22 women, and phenotype 4 in 13 women.

**Baseline characteristics of the PCOS and non-PCOS groups.** The baseline characteristics of the study group are shown in Table 1. The investigation and overall analysis of the study population as a whole showed no
differences in BMI or weight. The WC values were higher in the PCOS group; however, after the adjustment for age, BMI, and HOMA-IR score, this difference was no longer significant. Before and after the adjustment for possible confounding factors, the PCOS group had high serum concentrations of testosterone, androstenedione, and fasting insulin compared with the non-PCOS group. Participants with PCOS had higher FAI values; however, the difference was no longer significant postadjustment. However, HOMA-IR scores were higher in the PCOS group even after the adjustment for age and BMI.

FIGURE 1—Study chronogram. M, Monday; W, Wednesday; F, Friday; T, Tuesday; PAR-Q, Physical Activity Readiness Questionnaire; US, transvaginal pelvic ultrasonography; IRM test, one-repetition maximum test; DXA, dual-energy x-ray absorptiometry; RT, resistance training; SDC1, Supplemental Digital Content 1, progressive resistance training.

FIGURE 2—Study flow chart.
LH, FSH, estradiol, and SHBG concentrations did not differ between groups even after the adjustment for confounding covariates (see table, Supplemental Digital Content 2, linear regression mixed models, http://links.lww.com/MSS/A604).

Age and HOMA-IR were identified as potential confounders in the LMM and, therefore, were controlled in quantification analysis. HOMA-IR scores have been strongly associated with skeletal muscle mass and IR in women with PCOS (29), and age has been shown to be associated with progressive changes in skeletal muscle mass that contributes to decreased muscle function (13). Regression analysis showed that these covariates were effect modifiers ($P < 0.01$). After adjustment, both total LM and trunk LM were higher in the PCOS group than that in the non-PCOS group, but no differences were observed in the muscle mass index and %BF (Table 2).

Effects of exercise training. Preliminary comparisons between the PCOS and non-PCOS groups after the PRT protocol revealed no significant differences in weight, BMI, or WC. Among the measured hormonal parameters, the PCOS group showed high concentrations of androstenedione ($P < 0.01$) and FAI ($P = 0.03$) and reduced SHBG ($P = 0.03$) concentrations with no differences in testosterone concentrations, whereas the metabolic profile revealed higher insulin concentrations ($P = 0.02$) and HOMA-IR scores ($P = 0.03$), and no changes in glyceremia were seen in the PCOS group. After adjusting for age, BMI, and HOMA-IR, no inter- or intragroup differences were observed for weight and BMI. WC values did not differ significantly between groups but were reduced overall ($P < 0.01$) and in the PCOS group compared with baseline values ($P < 0.01$). Testosterone concentrations were reduced in the entire study population ($P < 0.01$), which were reduced in both groups with no significant differences between them (PCOS, $P < 0.01$; non-PCOS, $P < 0.01$). Androstenedione concentrations were increased in the PCOS group ($P < 0.01$) compared with the non-PCOS group and baseline values (PCOS, $P < 0.01$; non-PCOS, $P = 0.05$) for the entire study population ($P < 0.01$).

The metabolic profile revealed reduced SHBG concentrations in the entire group ($P < 0.01$) and the PCOS group (PCOS, $P = 0.01$; non-PCOS, $P = 0.07$) compared with baseline values. After PRT, the glycemia was reduced in the whole group ($P < 0.01$) and improved in both groups individually (PCOS, $P < 0.01$; non-PCOS, $P = 0.03$) with no intragroup differences. After adjusting for age and BMI, intra- and intergroup analyses revealed no statistically significant differences in serum insulin concentrations or HOMA-IR (see table, Supplemental Digital Content 2, linear regression mixed models, http://links.lww.com/MSS/A604).

The total LM and trunk LM did not differ within groups but remained higher in the PCOS group ($P = 0.01$, both) compared with baseline values. After PRT, appLM/height$^2$ ($P = 0.03$) and LM/height$^2$ ($P < 0.01$) were also higher in the PCOS group compared with baseline values. No difference was observed in %BF (Table 2). LM/height$^2$ was also increased in the PCOS group compared with the non-PCOS group (PCOS, $P = 0.04$; non-PCOS, $P = 0.77$) and appLM/height$^2$ (PCOS, $P = 0.05$; non-PCOS, $P = 0.82$—no significant difference) (Table 3) (see figure, Supplemental Digital Content 3, individual response of LM and muscle mass index pre- versus postintervention, http://links.lww.com/MSS/A605).

Correlations. The correlations are presented in Table 4. At the baseline, all of the LMM variables were correlated with HOMA-IR in the PCOS and non-PCOS groups. After PRT, only LM/height$^2$ did not correlate with HOMA-IR ($P = 0.15$) in the PCOS group. A change in LM/height$^2$ (a variable that differed between periods) with PRT in PCOS subjects was not correlated with a change in HOMA-IR ($P = 0.33$), although both values increased from the baseline, but a significant difference was seen only in LM/height$^2$ (see figure, Supplemental Digital Content 4, correlations between LM/height$^2$ and HOMA-IR in PCOS women, http://links.lww.com/MSS/A606).

Reproductive function. The reproductive function data in this study were included only for women with PCOS because PCOS is currently recognized as the leading cause of anovulatory infertility (28). Among women eligible for

**TABLE 1. Characteristics of the women with PCOS and the non-PCOS.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Mean (SD)</th>
<th>Mean (SD) after Adjustment</th>
<th>Baseline Mean (SD)</th>
<th>Mean (SD) after Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>73.1 (15.6)</td>
<td>72.6 (14.8)</td>
<td>68.1 (15.4)</td>
<td>67.9 (14.7)</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>28.4 (6.0)</td>
<td>28.2 (5.6)</td>
<td>26.2 (5.7)</td>
<td>26.2 (5.4)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>81.7 (12.8)$^{abc}$</td>
<td>80.5 (1.8)</td>
<td>78.2 (11.3)</td>
<td>75.8 (10.7)$^{a}$</td>
</tr>
<tr>
<td>LH (mU/mL$^{-1}$)</td>
<td>7.05 (7.4)</td>
<td>7.23 (6.8)</td>
<td>6.40 (6.2)</td>
<td>6.92 (6.6)</td>
</tr>
<tr>
<td>FSH (mU/mL$^{-1}$)</td>
<td>4.71 (2.8)</td>
<td>4.83 (3.2)</td>
<td>4.83 (2.8)</td>
<td>4.64 (3.7)</td>
</tr>
<tr>
<td>Estradiol (pg/mL$^{-1}$)</td>
<td>119.8 (85.2)</td>
<td>107.1 (68.5)</td>
<td>128.5 (83.7)</td>
<td>142 (89.9)</td>
</tr>
<tr>
<td>Androstenedione (ng/mL$^{-1}$)</td>
<td>120 (43.6)$^{abc}$</td>
<td>139.2 (54.7)$^{a}$</td>
<td>98.8 (32.5)</td>
<td>111 (33.4)$^{a}$</td>
</tr>
<tr>
<td>Testosterone (ng/mL$^{-1}$)</td>
<td>90 (35.1)$^{abc}$</td>
<td>72.8 (24.5)</td>
<td>74.4 (29.3)</td>
<td>62.6 (21.9)$^{a}$</td>
</tr>
<tr>
<td>SHBG (nmol/L$^{-1}$)</td>
<td>54.9 (37.8)$^{a}$</td>
<td>43.8 (24.4)$^{a}$</td>
<td>63.0 (36.7)</td>
<td>57.7 (35.5)$^{a}$</td>
</tr>
<tr>
<td>FAI</td>
<td>8.3 (3.3)$^{abc}$</td>
<td>7.6 (5.1)$^{a}$</td>
<td>5.6 (4.6)</td>
<td>5.3 (4.6)</td>
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<tr>
<td>Fasting glucose (mg/dL$^{-1}$)</td>
<td>96.2 (16.4)</td>
<td>91.1 (17.6)</td>
<td>95.7 (17.5)</td>
<td>90.6 (11.5)$^{a}$</td>
</tr>
<tr>
<td>Insulin (μU/mL$^{-1}$)</td>
<td>9.3 (6.9)$^{a}$</td>
<td>10.0 (8.7)$^{a}$</td>
<td>5.2 (4.5)</td>
<td>5.7 (4.3)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.27 (1.9)$^{a}$</td>
<td>2.47 (2.9)$^{a}$</td>
<td>1.26 (1.24)</td>
<td>1.32 (1.08)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD).
Same letters represent statistical differences ($P < 0.05$).
PCOS versus non-PCOS: $^a$baseline; $^b$after.
Baseline versus after: $^c$PCOS group; $^d$non-PCOS group; $^e$whole group.
PRT in this study, data were obtained from the 45 who completed the PRT protocol, including those who were excluded for pregnancy during the study. At the baseline, 24 subjects reported menstrual irregularities (anovulatory or amenorrheic), whereas 22 had regular ovulating periods. Of the 24 subjects with menstrual irregularities, one became pregnant and was excluded from the study and 17 reported improved menstrual cyclicity. Two women from the ovulatory PCOS group became pregnant and were excluded. Three volunteers became pregnant 1 month after completing the study (two from the anovulatory group and one from the ovulatory group).

**DISCUSSION**

The findings of this study reinforce the positive effects of PRT on body composition (visceral fat loss and increased LMM) in women who reported no changes in weight or BMI. Additionally, 16 wk of PRT resulted in reduced serum concentrations of testosterone and fasting glucose in all women (PCOS and non-PCOS) who were not hyperglycemic. There have been reports on exercise interventions and changes in lifestyle in women with PCOS, but only a few reports have examined the effects of resistance exercise in these women (9). These studies prescribed PRT with aerobic training and nutrition classes or nutrition advice (2,4,27,45,47) with varying results. To our knowledge, the current study is one of the first to examine the isolated effects of PRT on specific clinical outcomes in PCOS.

In this study, the PCOS group had high serum concentrations of testosterone and reduced insulin sensitivity compared with the non-PCOS group. Insulin metabolism disorders and IR are characteristic of metabolic syndrome in women with PCOS (39). Before PRT, the insulin concentrations and HOMA-IR scores in our study were higher in the PCOS group than that in the non-PCOS group. However, our data demonstrate that the PRT intervention had no effect on insulin sensitivity or concentrations in women with PCOS after adjusting for confounding covariables. Bruner et al. (4) observed reduced serum concentrations of insulin in the experimental group of participants with PCOS who received nutrition counseling in addition to performing physical exercise.

PRT also reduced fasting glucose concentrations in all participants regardless of the group. Although the reduction occurred in the entire cohort, most of the exercise-induced benefits of glucose homeostasis were observed in the PCOS group. Differences in the effects of strength training on glucose tolerance may be related to population differences. To evaluate the influence of resistance exercise training on glucose control in women with T2D, Fenicchia et al. (19) observed in a control group that subjects with high initial glucose concentrations showed the greatest exercise-induced benefits compared with individuals with normal glucose concentrations, who showed no exercise-induced changes.

We did not observe differences in estradiol concentrations between groups or in association with the training program.
In contrast, with decreased total testosterone and FAI concentrations (although with no significant differences, especially in the PCOS group), SHBG concentrations decreased and androstenedione concentrations increased after PRT in women with PCOS. By increasing LMM and decreasing visceral adiposity, PRT may negatively influence aromatase activity, which would explain the increased androstenedione concentrations in the PCOS group, because androstenedione is the major substrate for this enzyme and is a precursor of sex hormones such as testosterone and estrogen (18). Thomson et al. (46,47) also observed reduced testosterone and fasting glucose concentrations after intervention in the study group that received nutrition counseling in addition to performing physical exercise.

In this study, the WC values in the PCOS group were higher than those in the non-PCOS group at the baseline; this difference was likely because most of the women in the PCOS group were obese or overweight, and the difference disappeared after the adjustment for BMI and age. After PRT, all participants had reduced WC values regardless of the group and PCOS status. WC reductions were also observed in other studies (3,28,46,47). WC is an important predictor of central obesity-related health risks (25), and its reduction reinforces the positive correlation between physical exercise and health. Although we did not observe BMI differences, other studies have suggested that WC is the best predictor of obesity-related health risks because overweight, obese, and normal-weight individuals have comparable rates of hypertension, T2D, dyslipidemia, and metabolic syndrome (25). Obesity, mainly visceral obesity, is a severe risk factor for cardiovascular and glucose–insulin disorders that result in several pathophysiological changes such as a lower hepatic insulin extraction with increased hepatic production of glucose and a reduced glucose uptake by the muscle tissue (30). This visceral fat has been implicated in the etiology of IR in PCOS (23).

Furthermore, baseline trunk LM and total LM were increased in women with PCOS compared with non-PCOS women. Other studies comparing LM in different PCOS phenotypes reported that the same variables were higher in women with classic PCOS, which was associated with obesity, central obesity, and IR (29). Carmina et al. (7) also found increased LMM only in obese women with PCOS, which correlated with fat mass and insulin but not androgen concentrations. In this study, statistical modeling considered HOMA-IR as an LMM-modifying covariate and was, therefore, controlled in the adjustments. Although the correlations between HOMA-IR and LMM variables are implicit in the regression models used, a correlation was detected between HOMA-IR and LM in the PCOS and non-PCOS groups. These observations suggest that the hyperandrogenism that is prevalent in PCOS is responsible for the LMM differences. The association between increased LMM and IR may be due to hyperandrogenism and increased LM and IR. The positive correlation between insulin and androgen concentrations in women with PCOS is already known, wherein

<table>
<thead>
<tr>
<th>Table 3. Intragroup: LM, muscle mass index, and total %BF in PCOS and non-PCOS women pre- and postexercise.</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td><strong>PCOS (45)</strong></td>
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<tr>
<td>Total LM (g)**</td>
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<tr>
<td>Estimated Difference (95% CI)</td>
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<tr>
<td>Trunk LM (g)<strong>,</strong>*</td>
</tr>
<tr>
<td>Estimated Difference (95% CI)</td>
</tr>
<tr>
<td>LM/height2 (kg·m⁻²)<strong>,</strong>*</td>
</tr>
<tr>
<td>Estimated Difference (95% CI)</td>
</tr>
<tr>
<td>AppLM/height2 (kg·m⁻²)<strong>,</strong>*</td>
</tr>
<tr>
<td>Estimated Difference (95% CI)</td>
</tr>
<tr>
<td>%BF</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) and CI.

*P < 0.05, PCOS + non-PCOS, after training. **Age, ***HOMA-IR, significant covariate, P < 0.05.
hyperinsulinemia induces increased androgen production, which in return contributes to IR in the adipose tissue and skeletal muscle (5).

Resistance exercise is defined as skeletal muscle contractions that result in increased muscle mass and strength (36), and androgens are known to have direct anabolic effects on skeletal muscle. The effect of testosterone on the muscle involves several mechanisms, including the induction of protein synthesis and recruitment of satellite cells (37). However, previous studies have stated that changes in insulin and androgen concentrations affect not only muscle quantity but also may affect muscle quality by decreasing the ratio between muscle fibers and higher insulin sensitivity (Type I) to lower sensitivity fibers (Types IIA and IIX) (24).

The current study revealed that PRT induced increased LMM only in the PCOS group but resulted in no important changes in IR. In agreement with our findings, Comerford et al. (11) reported that different treatment approaches that increase muscle mass may affect IR differently depending on the corresponding changes in the intrinsic muscle quality. Women with PCOS develop hyperinsulinemia to compensate for a physiologically important defect in insulin receptor signaling that is independent of obesity and T2D (17), which shows that the increase in muscle mass may not be the cause of IR but a consequence of compensatory hyperinsulinemia (11). In the present study, the increase in LMM in women with PCOS was not associated with HOMA-IR after PRT.

The decrease in glucose most likely had limited clinical relevance because our patients were normoglycemic women with PCOS. However, increased LM after PRT may be an important mediator of improved glycemic control; the possible mechanisms for this may include an enhanced muscle contraction-induced glucose uptake or increased glucose transport molecules type 4 (GLUT4) and insulin signaling in the skeletal muscles of patients with T2D (40), but this is not known for PCOS. Increased muscle fiber volume may be a mechanism for increased GLUT4 expression (21). However, the metabolic profile of muscle fibers is determined by insulin sensitivity, receptor quantity, specific uptake system activity, and substrate metabolism (35), all of which are changed in PCOS.

Thomson et al. (46,47) concluded that physical exercise resulted in beneficial changes in LMM and reduced body weight. No changes in body weight and BMI were observed in our study; however, it was highlighted in two other studies (2,28) in which the prescribed PRT was not well reported. Loss of visceral fat without weight loss is possible if there is a simultaneous increase in LMM during the physical exercise program (20), which suggests that a physically active person with adequate muscle mass may not be of normal weight but may still have a reduced risk of cardiovascular disease (15).

Although we did not specifically evaluate ovulation, anovulatory women with PCOS in our study had improved menstrual function after the second month of PRT; several women were excluded because of pregnancy, and pregnancy after study participation was also reported in anovulatory women with PCOS. Several other studies (2,47) reported improved menstrual and/or ovulation frequency after PRT. Aubuchon et al. (2) observed a 46% pregnancy rate in their study after intervention; however, they attributed this response to weight loss. In a study by Thomson et al. (47), 49% of participants reported an overall improvement in ovulation and/or menstrual cyclicity after intervention with no differences between the diet-only and diet plus exercise groups. In addition to weight reduction, the authors observed reduced abdominal fat and WC values with no hormonal changes between women with improved reproductive function and those without. Other studies suggested that weight reduction is most important for the reestablishment of ovulation in women with PCOS as well as improved insulin sensitivity (22,26). However, we did not observe any changes in those variables with PRT intervention. The reestablishment of ovulation may be related to changes in androgen concentrations and body composition in women with PCOS. Changes in serum testosterone and FAI concentrations after PRT might enhance ovarian function because elevated free-circulating androgen concentrations are associated with polycystic ovaries, which might lead to chronic anovulation.

The sample loss during the intervention was greater than expected, which reduced the sample size. There was a significant change in body composition, which can improve hyperandrogenism and reproductive function. Although the women studied here were not hyperglycemic, reduced glucose concentrations were observed in the group as a whole. The metabolic variables such as insulin, HOMA, and SHBG concentrations did not demonstrate the expected changes. Theoretically, one would expect that increased lean body mass — increased insulin-sensitive tissue mass would result in increased insulin sensitivity.

One limitation of the current study was that we did not analyze the habitual physical activity levels related to work and leisure time. However, the sample population was composed of volunteers without consistent supervised physical activity. Another limitation was that the indirect assessment of IR (HOMA) may not have been sensitive enough to detect the effects of exercise, and a more sensitive assessment may have been more appropriate, such as the

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**TABLE 4. Correlations of HOMA-IR with variables of LMM in PCOS.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>After</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS</td>
<td>non-PCOS</td>
<td>PCOS</td>
<td>non-PCOS</td>
</tr>
<tr>
<td>$r$</td>
<td>$P$ value</td>
<td>$r$</td>
<td>$P$ value</td>
</tr>
<tr>
<td>Total LM (g)</td>
<td>0.694</td>
<td>&lt;0.01</td>
<td>0.421</td>
</tr>
<tr>
<td>Trunk LM (g)</td>
<td>0.682</td>
<td>&lt;0.01</td>
<td>0.470</td>
</tr>
<tr>
<td>LM/height$^2$ (kg m$^{-2}$)</td>
<td>0.702</td>
<td>&lt;0.01</td>
<td>0.422</td>
</tr>
<tr>
<td>AppLM/height$^2$ (kg m$^{-2}$)</td>
<td>0.672</td>
<td>&lt;0.01</td>
<td>0.432</td>
</tr>
</tbody>
</table>

*Note: Table**

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hyperinsulinemic–euglycemic clamp technique (the gold standard for assessing insulin action), oral glucose tolerance test, which identifies a larger number of glucose metabolism abnormalities than the fasting glucose, or measurement of GLUT4 concentrations, which assesses the glucose uptake; also, in the present study, skeletal muscle biopsies, which measure changes in muscle fiber size before and after PRT, were not performed. The initial project design did not include analysis of these markers. In addition, in this study, we used immunoassays for the measurement of steroid sex hormones, which may not be as sensitive as mass spectrometry for detecting androgen levels in women. However, the strengths of this study include supervised exercise; unlike previous studies, our study specifically investigated the isolated effects of PRT using an independent control group to compare the effects of exercise in women with PCOS.

CONCLUSIONS

In the present study, PRT alone effectively improved hyperandrogenism, reproductive function, and body composition in women with PCOS. The decreased WC and increased LMM underscore the fact that weight reduction need not be the end point of exercise. No further metabolic improvements were observed. These results suggest that lifestyle changes and PRT comprise a treatment strategy for women with PCOS. However, further research is required to elucidate the effect of strength training in IR states in women with PCOS.

We thank all of the participants who volunteered for this study. We appreciate their willingness to exercise with unwavering intensity and to sacrifice many of their normal activities to adhere to the described protocol. We also thank the members of the Centre of Physical Education, Recreation, and Sports at the University of São Paulo and members of the Department of Obstetrics and Gynecology (FMERP-USP), and the sector of assisted human reproduction, especially Océlia de Vasconcelos for blood collection and Cristiana Carolina Padovan for technical support. The São Paulo State Research Foundation (FAPESP—process 10/08800-8) and Coordination for the Improvement of Higher Education Personnel (CAPES) funded this study.

The authors have no conflicts of interest to declare. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

REFERENCES


